

# **PROPOSITION 65 BACKGROUND DOCUMENT**

## **PUBLIC WORKSHOP ON DEVELOPING SAFE HARBOR NUMBERS**

**October 2000**



**Reproductive and Cancer Hazard Assessment Section  
Office of Environmental Health Hazard Assessment  
California Environmental Protection Agency**

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## Proposition 65 Safe Harbor Development

The Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency is the lead agency for the implementation of the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65 or the Act). In that role, OEHHA has developed Proposition 65 safe harbor levels -- no significant risk levels (NSRLs) for carcinogens and maximum allowable daily levels (MADLs) for chemicals that cause reproductive toxicity. The NSRL is the daily intake level calculated to result in one excess case of cancer in an exposed population of 100,000, assuming lifetime exposure at the level in question. The MADL is the highest level at which the chemical would have no observable adverse reproductive effect assuming exposure at 1,000 times that level. The NSRLs and MADLs are promulgated in Title 22, California Code of Regulations (CCR), Sections 12705 and 12805 to assist interested parties in determining whether warnings are required for exposures to listed chemicals, and whether discharges of that chemical to sources of drinking water are prohibited. If an exposure subject to the Act can be shown to be less than the specific regulatory level, the responsible person has "safe harbor" from the warning requirement and discharge prohibition. The availability of a safe harbor level provides greater certainty to responsible parties in complying with the Act and to the public in determining which exposures and discharges are of concern.

A three-tiered process for development of NSRLs is currently in place. NSRLs may be based on:

- *de novo* dose response assessments conducted by OEHHA (22 CCR §12705(b))
- assessments conducted by another state or federal agency (22 CCR §12705(c)), or
- expedited assessments conducted by OEHHA (22 CCR §12705(d)).

The process for development of MADLs is described in 22 CCR §12803. Further specification of procedures used and assumptions made in developing safe harbor numbers are set out in regulation (See Appendix I).

Due to a series of budget cuts in the mid-1990s, OEHHA has had insufficient resources for development of safe harbor levels. A recent budget augmentation has provided OEHHA with funds to resume this activity. In preparation for implementing a program to derive NSRLs and MADLs, OEHHA is holding a public workshop to obtain input from interested parties.

Ideally, a safe harbor level should be derived for each chemical listed under Proposition 65 as causing cancer or reproductive toxicity. In practice, however, only a subset of the listed chemicals can be assessed at any particular time. OEHHA is committed to developing 20-35 safe harbor levels per year, using the processes described above.

The needs of the regulated community and the public are important in determining how the large number of chemicals requiring assessment should be addressed. OEHHA

welcomes comments on this issue and will take suggestions into consideration in ordering chemicals for safe harbor development. OEHHA proposes that if an interested party wishes to have a specific chemical assessed, the interested party make that request in writing and provide a rationale for why the assessment of that chemical is needed. OEHHA welcomes suggestions on alternative methods for the public to make such a request.

Some of the factors OEHHA considers in ordering chemicals for safe harbor development include the availability of dose response data, public input, and resources required to perform any particular dose response assessment. In accordance with the settlement agreement in the case of AFL-CIO et al. v. Deukmejian (Sacramento Superior Court No. 3481295), priority lists for development of safe harbor levels (i.e., NSRLs) were periodically released (OEHHA, 1993, 1994). The most recent list was included in the 1994 *Status Report* on safe harbor development (OEHHA, 1994). OEHHA has now updated the 1994 *Status Report* and has included it in this document as Appendix II. Appendix II is comprised of the following four tables:

Table A -- a list of NSRLs adopted in regulation for carcinogens (22 CCR §12705),

Table B -- a list of MADLs adopted in regulation for chemicals causing reproductive toxicity (22 CCR §12805),

Table C -- a priority list for the development of NSRLs, and

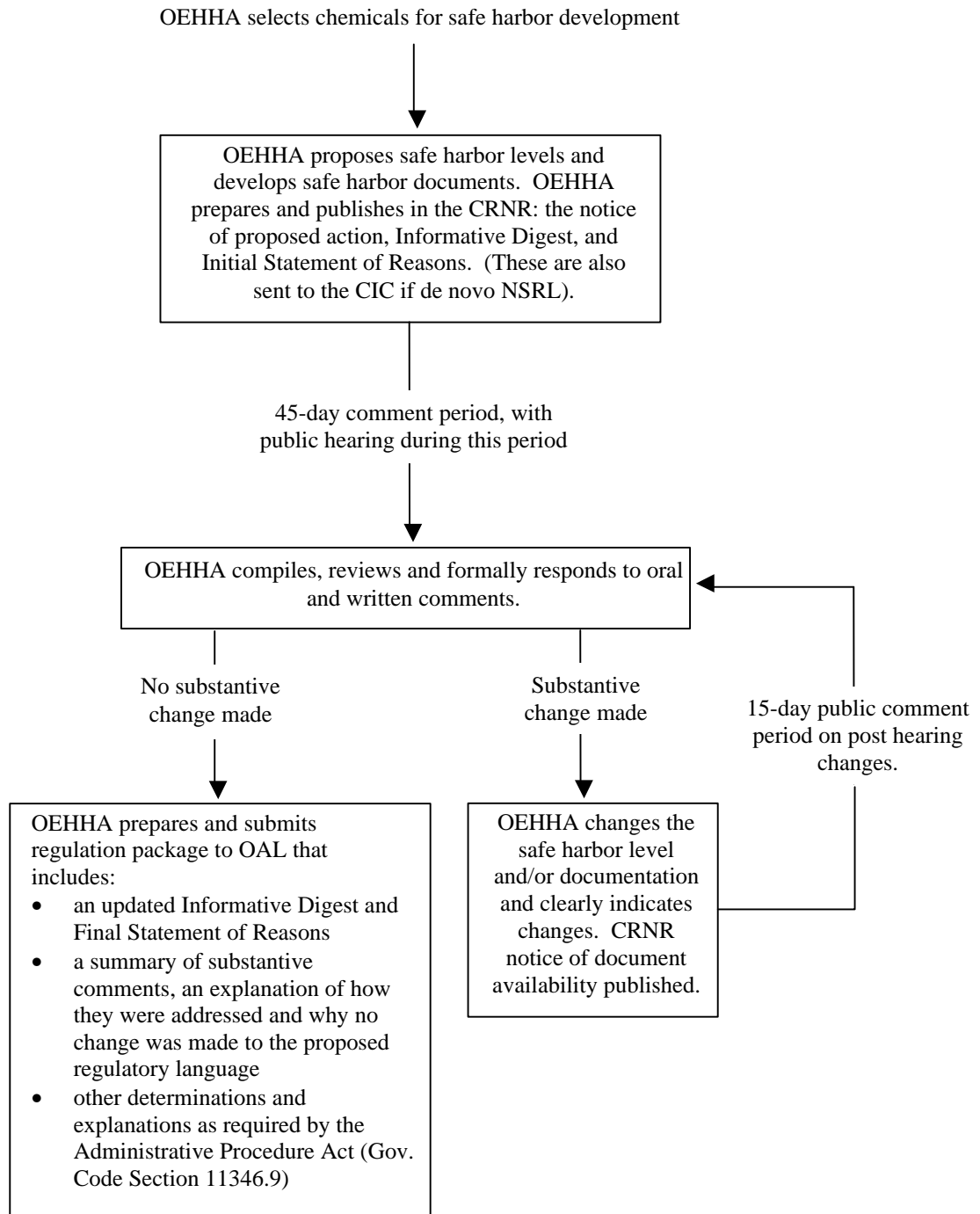
Table D -- a priority list for the development of MADLs.

The listing of the chemicals in Tables C and D is based on the speed with which OEHHA anticipates completion of the NSRLs or MADLs given data availability, along with public input, resources, and priorities in the settlement agreement. Requests from interested parties for specific chemicals will be given serious consideration in ordering chemicals for the development of safe harbor levels.

Pursuant to the settlement agreement, OEHHA plans to routinely release an updated priority list. OEHHA intends this program to assist businesses with compliance with Proposition 65. Comments on how OEHHA can optimally assist interested parties are sought at this workshop and in writing.

Regulatory guidance for the process by which safe harbor levels are developed is provided in 22 CCR Sections 12701-12705 and 12801-12803 and the Administrative Procedure Act (Government Code Section 11340 *et seq.*), as summarized in Figure 1.

**Figure 1. Safe Harbor Development.**



CIC: Carcinogen Identification Committee  
NSRL: No Significant Risk Level

The workshop to discuss these issues will be held on November 15, 2000, in Training Room B at the Elihu Harris State Building, 1515 Clay Street in downtown Oakland. The workshop will begin at 10 a.m. and end when all business is conducted or at 5 p.m.

Questions concerning the workshop and comments on issues discussed above may be directed to: Ms. Cynthia Oshita, Office of Environmental Health Hazard Assessment, 301 Capitol Mall, 2<sup>nd</sup> Floor, Room 205, Sacramento, California 95814. Ms. Oshita's telephone number is (916) 445-6900, and fax number is (916) 327-1097. OEHHA would appreciate receiving any written comments by December 8, 2000.

## **References**

American Federation of Labor and Congress of Industrial Organizations, the Natural Defense Council, Environmental Defense Fund, Sierra Club, Public Citizen, Inc., Campaign California, Citizens for a Better Environment, Silicon Valley Toxics Coalition, Bernardo Huerta v. Deukmejian. Settlement Agreement. Sacramento Superior Court No. 3481295. 1992.

Office of Environmental Health Hazard Assessment (OEHHA, 1993). Priority List for the Development of Carcinogen Dose Response Assessment for Proposition 65. OEHHA, Sacramento, CA, January 1993.

Office of Environmental Health Hazard Assessment (OEHHA, 1994). Safe Drinking Water and Toxic Enforcement Act of 1986 (Prop. 65). No Significant Risk Levels for Carcinogens. Acceptable Intake Levels for Reproductive Toxicants. Status Report. Part C, OEHHA, Sacramento, CA, January 1994.

## **Proposition 65 Regulations Governing the Development of Safe Harbor Levels**

### **TITLE 22. Chapter 3. Safe Drinking Water and Toxic Enforcement Act of 1986**

#### **Article 7. No Significant Risk Levels**

##### **§12701. General.**

(a) The determination of whether a level of exposure to a chemical known to the state to cause cancer poses no significant risk for purpose of Health and Safety Code Section 25249.10(c) shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for the listing of the chemical as known to the state to cause cancer. Nothing in this article shall preclude a person from using evidence, standards, risk assessment methodologies, principles, assumptions or levels not described in this article to establish that a level of exposure to a listed chemical poses no significant risk.

(b) A level of exposure to a listed chemical, assuming daily exposure at that level, shall be deemed to pose no significant risk provided that the level is determined:

(1) By means of a quantitative risk assessment that meets the standards described in Section 12703,

(2) By application of Section 12707 (Routes of Exposure); or

(3) By one of the following, as applicable:

(A) If a specific regulatory level has been established for the chemical in question in Section 12705, by application of that level.

(B) If no specific level is established for the chemical in question in Section 12705, by application of Section 12709 (Exposure to Trace Elements) or 12711 (Levels Based on State or Federal Standards) unless otherwise provided.

(c) The chemicals, routes of exposure and conditions of use specifically listed in this article do not include all chemicals, routes of exposure and conditions of use that pose no significant risk. The fact that a chemical, route of exposure or condition of use does not appear in this article does not mean that it poses a significant risk.

(d) This article establishes exposure levels posing no significant risk solely for purposes of Health and Safety Code Section 25249.10(c). Nothing in this article shall be construed to establish exposure or risk levels for other regulatory purposes.

##### **§12703. Quantitative Risk Assessment.**

(a) A quantitative risk assessment which conforms to this section shall be deemed to determine the level of exposure to a listed chemical which, assuming daily exposure at that level, poses no significant risk. The assessment shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for listing the chemical as known to the state to cause cancer. In the absence of principles or assumptions scientifically more appropriate, based upon the available data, the following default principles and assumptions shall apply in any such assessment:

(1) Animal bioassay studies for quantitative risk assessment shall meet generally accepted scientific principles, including the thoroughness of experimental protocol, the degree to which dosing resembles the expected manner of human exposure, the temporal exposure pattern, the duration of study, the purity of test material, the number and size of exposed groups, the route of exposure, and the extent of tumor occurrence.

(2) The quality and suitability of available epidemiologic data shall be appraised to determine whether the study is appropriate as the basis of a quantitative risk assessment, considering such factors as the selection of the exposed and reference groups, reliable ascertainment of exposure, and completeness of follow-up. Biases and confounding factors shall be identified and quantified.

(3) Risk analysis shall be based on the most sensitive study deemed to be of sufficient quality.

(4) The results obtained for the most sensitive study deemed to be of sufficient quality shall be applicable to all routes of exposure for which the results are relevant.

(5) The absence of a carcinogenic threshold dose shall be assumed and no-threshold models shall be utilized. A linearized multistage model for extrapolation from high to low doses, with the upper 95 percent confidence limit of the linear term expressing the upper bound of potency shall be utilized. Time-to-tumor models may be appropriate where data are available on the time of appearance of individual tumors, and particularly when survival is poor due to competing toxicity.

(6) Human cancer potency shall be derived from data on human or animal cancer potency. Potency shall be expressed in reciprocal milligrams of chemical per kilogram of bodyweight per day. Interspecies conversion of animal cancer potency to human cancer potency shall be determined by multiplying by a surface area scaling factor equivalent to the ratio of human to animal bodyweight, taken to the one-third power. This is equivalent to a scaling factor of 14 when extrapolating from mouse data, and a scaling factor of 6.5 when extrapolating from rat data.

(7) When available data are of such quality that physiologic, pharmacokinetic and metabolic considerations can be taken into account with confidence, they may be used in the risk assessment for inter-species, inter-dose, and inter-route extrapolations.

(8) When the cancer risk applies to the general population, human body weight of 70 kilograms shall be assumed. When the cancer risk applies to a certain subpopulation, the following assumptions shall be made, as appropriate:

Subpopulation	Kilograms of Body Weight
Man (18+ years of age)	70
Woman (18+ years of age)	58
Woman with conceptus	58
Adolescent (11-18 years of age)	40
Child (2-10 years of age)	20
Infant (0-2 years of age)	10

(b) For chemicals assessed in accordance with this section, the risk level which represents no significant risk shall be one which is calculated to result in one excess case of cancer in an exposed population of 100,000, assuming lifetime exposure at the level in question, except where sound considerations of public health support an alternative level, as, for example:

- (1) where chemicals in food are produced by cooking necessary to render the food palatable or to avoid microbiological contamination; or
- (2) where chlorine disinfection in compliance with all applicable state and federal safety standards is necessary to comply with sanitation requirements; or
- (3) where a clean-up and resulting discharge is ordered and supervised by an appropriate governmental agency or court of competent jurisdiction.

#### §12705. Specific Regulatory Levels Posing No Significant Risk.

(a) Daily exposure to a chemical at a level which does not exceed the level set forth in subsections (b), (c) and (d) for such chemical shall be deemed to pose no significant risk within the meaning of Health and Safety Code section 25249.10 (c).

(b) Levels of exposure deemed to pose no significant risk may be determined by the lead agency based on a risk assessment conducted by the lead agency pursuant to the guidelines set forth in Section 12703, or a risk assessment reviewed by the lead agency and determined to be consistent with the guidelines set forth in Section 12703.

(1) The following levels based on risk assessments conducted or reviewed by the lead agency shall be deemed to pose no significant risk:

(b) Chemical Name	Level (micrograms/day)
Acrylonitrile	0.7
Aldrin	0.04
Arsenic	0.06 (inhalation)
Asbestos	100 fibers inhaled/day*
Benzene	7
Benzidine	0.001
Bis(2-chloroethyl)ether	0.3
Bis(chloromethyl)ether	0.02
Butylated hydroxyanisole	4000
Cadmium	0.05 (inhalation)



Carbon tetrachloride	5
Chromium (hexavalent compounds)	0.001 (inhalation)
DDT, DDE and DDD (in combination)	2
1,2-Dibromo-3-chloropropane (DBCP)	0.1
para-Dichlorobenzene	20
3,3'-Dichlorobenzidine	0.6
Dichloromethane (Methylene chloride)	200 (inhalation)
Dieldrin	0.04
1,4-Dioxane	30
Epichlorohydrin	9
Ethylene dibromide	0.2 (ingestion) 3 (inhalation)
Ethylene dichloride	10
Ethylene oxide	2
Hexachlorobenzene	0.4
Hexachlorodibenzodioxin	0.0002
Hexachlorocyclohexane (technical grade)	0.2
N-Nitroso-n-dibutylamine	0.06
N-Nitrosodiethylamine	0.02
N-Nitrosodimethylamine	0.04
N-Nitrosodiphenylamine	80
N-Nitrosodi-n-propylamine	0.1
N-Nitroso-N-ethylurea	0.03
N-Nitroso-N-methylurea	0.006
Polybrominated biphenyls	0.02
2,3,7,8-Tetrachlorodibenzo-p-dioxin	0.000005
Toxaphene	0.6
Trichloroethylene	50 (ingestion) 80 (inhalation)
2,4,6-Trichlorophenol	10
Urethane	0.7
Vinyl chloride	3

\*Fibers equal to or greater than 5 micrometers in length and 0.3 micrometers in width, with a length to width ratio of greater than or equal to 3:1 as measured by phase contrast microscopy.

(2) Whenever the lead agency proposes to formally adopt, pursuant to this subsection, a level which shall be deemed to pose no significant risk of cancer, assuming daily exposure at that level, the lead agency shall provide to each member of the Scientific Advisory Panel notice of the proposed action, a copy of the proposed level, and a copy of the initial statement of reasons supporting the proposal. The close of the public comment period for any such proposal shall be scheduled by the lead agency so as to permit the Scientific Advisory Panel the opportunity to review such proposal and provide comment to the lead agency. Any such comment by the Scientific Advisory Panel shall become a part of the formal rulemaking file. Nothing in this subsection shall be construed to prevent members of the Scientific Advisory Panel from providing comments individually on any such proposal, or to require the Scientific Advisory Panel to submit any comment.

(c) Unless a specific regulatory level for a chemical known to the state to cause cancer has been established in subsection (b), levels of exposure deemed to pose no significant risk may be determined by the lead agency based on state or federal risk assessments.

(1) Any interested party may request the lead agency to reevaluate a level established in this subsection based on scientific considerations that indicate the need for the lead agency to develop its own risk assessment or to conduct a detailed review of the risk assessment used to derive the level in question. Such request shall be made in writing, and shall include a description of the scientific considerations that indicate the need for the lead agency to develop its own risk assessment or to conduct a detailed review of the risk assessment used to derive the level in question. The lead agency may establish a level for the chemical in question in subsection (b) as it deems necessary.

(2) The following levels based on state or federal risk assessments shall be deemed to pose no significant risk:

Chemical Name	Level (micrograms/day)
Acrylonitrile	0.7
Acetaldehyde	90 (inhalation)
Acrylamide	0.2
Allyl chloride	30
Aniline	100
Azobenzene	6
Benzo[a]pyrene	0.06
Benzyl chloride	4
Beryllium oxide	0.1
Beryllium sulfate	0.0002
Bromodichloromethane	5
1,3-Butadiene	0.4
Chlordane	0.5
Chloroform	20 (ingestion) 40 (inhalation)
Coke oven emissions	0.3
DDVP (Dichlorvos)	2
Dichloromethane (Methylene chloride)	50
Di(2-ethylhexyl)phthalate	80
2,4-Dinitrotoluene	2
Folpet	200
Formaldehyde (gas)	40
Furmecyclo	20
Heptachlor	0.2
Heptachlor epoxide	0.08
Hexachlorocyclohexane	
alpha isomer	0.3
beta isomer	0.5
gamma isomer	0.6
Hydrazine	0.04
Hydrazine sulfate	0.2
4,4'-Methylene	
bis (N,N-dimethyl)benzeneamine	20
Nickel refinery dust	0.8
Nickel subsulfide	0.4
N-Nitrosodiethanolamine	0.3
N-Nitrosomethylethylamine	0.03
N-Nitrosopyrrolidine	0.3
Pentachlorophenol	40
Polychlorinated biphenyls (PCBs)	0.09
Tetrachloroethylene	14

(d) Unless a specific regulatory level has been established for a chemical known to the state to cause cancer in subsection (b) or (c), levels of exposure deemed to pose no significant risk may be determined by the lead agency using an expedited method consistent with the procedures specified in Section 12703.

(1) Any interested party may request the lead agency to reevaluate a level established in this subsection and to consider the adoption, in subsection (c), of a level based on a state or federal risk assessment. Such request shall be made in writing, and shall include a copy of the state or federal risk assessment which the interested party wishes the lead agency to consider as the basis for a level in subsection (c). The lead agency may establish a level in subsection (c) for the chemical in question based on a state or federal risk assessment as it deems necessary.

(2) Any interested party may request the lead agency to reevaluate a level established in this subsection based on scientific considerations that indicate the need for a conventional risk assessment. Such request shall be made in writing, and shall include a description of the scientific considerations that indicate the need for a conventional risk assessment. The lead agency may conduct a conventional risk assessment for the chemical in question, and establish a level in subsection (b) as it deems necessary.

(3) The following levels of exposure based on risk assessments conducted by the lead agency using an expedited method consistent with the procedures specified in Section 12703 shall be deemed to pose no significant risk:

Chemical Name	Level (micrograms/day)
A-alpha-C 2-Amino-9H-pyridol[2,3-b]indole	2
Acetamide	10
2-Acetylaminofluorene	0.2
Actinomycin D	0.00008
AF-2:[2-(2-furyl)-3(5-nitro-2-furyl)] acrylamide	3
2-Aminoanthraquinone	20
<i>o</i> -Aminoazotoluene	0.2
4-Aminobiphenyl (4-aminodiphenyl)	0.03
3-Amino-9-ethylcarbazole hydrochloride	9
1-Amino-2-methylantraquinone	5
2-Amino-5-(5-nitro-2-furyl) -1,3,4-thiadiazole	.04
Amitrole	0.7
<i>o</i> -Anisidine	5
<i>o</i> -Anisidine hydrochloride	7
Aramite	20
Auramine	0.8
Azaserine	0.06
Azathioprine	0.4
Benzyl violet 4B	30
beta-Butyrolactone	0.7
Captafol	5
Captan	300
Chlorambucil	0.002
Chlordecone (Kepone)	0.04
Chlorendic acid	8
Chlorinated paraffins (Average chain length, C12; approximately 60 percent chlorine by weight)	8
Chlorodibromomethane	7
Chloromethyl methyl ether (technical grade)	0.3
3-Chloro-2-methylpropene	5
4-Chloro-ortho-phenylenediamine	40
Chlorothalonil	200
p-Chloro- <i>o</i> -toluidine	3
Chlorozotocin	0.003
C. I. Basic Red 9 monohydrochloride	3
Cinnamyl anthranilate	200
<i>p</i> -Cresidine	5
Cupferron	3
Cyclophosphamide (anhydrous)	1
Cyclophosphamide (hydrated)	1
D&C Red No. 9	100
Dacarbazine	0.01
Daminozide	40
Dantron (Chrysazin; 1,8-Dihydroxyanthraquinone)	9

2,4-Diaminoanisole	30
2,4-Diaminoanisole sulfate	50
4,4'-Diaminodiphenyl ether (4,4'-Oxydianiline)	5
2,4-Diaminotoluene	0.2
Dibenz[a,h]anthracene	0.2
1,1-Dichloroethane	100
Diethylstilbestrol	0.002
Diglycidyl resorcinol ether (DGRE)	0.4
Dihydrosafrole	20
4-Dimethylaminoazobenzene	0.2
trans-2[Dimethylamino)methyliminol]-5- [2-(5-nitro-2-furyl)vinyl]- 1,3,4-oxadiazole	2
7,12-Dimethylbenz(a)anthracene	0.003
Dimethylcarbamyl chloride	0.05
1,2-Dimethylhydrazine	0.001
Dimethylvinylchloride	20
Direct Black 38 (technical grade)	0.09
Direct Blue 6 (technical grade)	0.09
Direct Brown 95 (technical grade)	0.1
Disperse Blue 1	200
Estradiol 17B	0.02
Ethyl-4,4'-dichlorobenzilate (chlorobenzilate)	7
Ethylene thiourea	20
Ethyleneimine	0.01
2-(2-Formylhydrazino)-4-(5-nitro-2- furyl)thiazole	0.3
Glu-P-1 (2-Amino-6-methyldipyrido [1,2-a:3',2'-d]imidazole)	0.1
Glu-P-2 (2-Aminodipyrido[1,2-a:3',2'-d]imidazole	0.5
Gyromitrin (Acetaldehyde methylformylhydrazone)	0.07
HC Blue 1	10
Hexachloroethane	20
Hydrazobenzene (1,2-Diphenylhydrazine)	0.8
IQ (2-Amino-3-methylimidazo[4,5-f]quinoline]	0.5
Lasiocarpine	0.09
Lead acetate	3
Lead subacetate	20
Me-A-alpha-C (2-Amino-3-methyl-9H-pyrido[2,3-b]indole)	0.6
Melphalan	0.005
3-Methylcholanthrene	0.03
4,4'-Methylene bis(2-chloroaniline)	0.5
4,4'-Methylene bis(2-methylaniline)	0.8
4,4'-Methylenedianiline	0.4
4,4'-Methylenedianiline dihydrochloride	0.6
Methyl methanesulfonate	7
2-Methyl-1-nitroanthraquinone (of uncertain purity)	0.2
N-Methyl-N'-nitro-N-nitrosoguanidine	0.08
Methylthiouracil	2
Michler's ketone	0.8
Mirex	0.04
Mitomycin C	0.00009
Monocrotaline	0.07
2-Naphthylamine	0.4
Nitrilotriacetic acid	100
Nitrilotriacetic acid, trisodium salt monohydrate	70
5-Nitroacenaphthene	6
5-Nitro-o-anisidine	10

Nitrofen (technical grade)	9
Nitrofurazone	0.5
1-[5-Nitrofurfurylidine)-amino]-2-imidazolidinone	0.4
N-[4-(5-Nitro-2-furyl)-2-thiazolyl] acetamide	0.5
p-Nitrosodiphenylamine	30
N-Nitroso-N-methylurethane	0.006
N-Nitrosomorpholine	0.1
N-Nitrosornicotine	0.5
N-Nitrosopiperidine	0.07
Phenacetin	300
Phenazopyridine	4
Phenazopyridine hydrochloride	5
Phenesterin	0.005
Phenobarbital	2
Phenoxybenzamine	0.2
Phenoxybenzamine hydrochloride	0.3
o-Phenylphenate, sodium	200
Ponceau MC (D&C Red No. 5)	200
Ponceau 3R (FD&C Red No. 1)	40
Potassium bromate	1
Procarbazine	0.05
Procarbazine hydrochloride	0.06
1,3-Propane sultone	0.3
beta-Propiolactone	0.05
Propylthiouracil	0.7
Reserpine	0.06
Safrole	3
Sterigmatocystin	0.02
Streptozotocin	0.006
Styrene oxide	4
Sulfallate	4
1,1,2,2-Tetrachloroethane	3
Thiocetamide	0.1
4,4'-Thiodianiline	0.05
Thiourea	10
Toluene diisocyanate	20
o-Toluidine	4
o-Toluidine hydrochloride	5
Tris(1-aziridinyl)phosphine sulfide (Thiotepa)	0.06
Tris(2,3-dibromopropyl)phosphate	0.3
Trp-P-1 (Tryptophan-P-1)	0.03
Trp-P-2 (Tryptophan-P-2)	0.2
Vinyl trichloride (1,1,2-Trichloroethane)	10

§12707. Routes of Exposure.

(a) Where scientifically valid absorption studies conducted according to generally accepted standards demonstrate that absorption of a chemical through a specific route of exposure can be reasonably anticipated to present no significant risk of cancer at levels of exposure not in excess of current regulatory levels, the lead agency may identify the chemical as presenting no significant risk by that route of exposure. Any exposure, discharge or release of a chemical so identified shall be deemed to present no significant risk to the extent that it results in exposure to humans by the identified route, and does not exceed the level established in any other applicable federal or state standard, regulation, guideline, action level, license, permit, condition, requirement or order.

(b) The following chemicals present no significant risk of cancer by the route of ingestion:

- (1) Asbestos
- (2) Beryllium and beryllium compounds

- (3) Cadmium and cadmium compounds
- (4) Chromium (hexavalent compounds)
- (5) Nickel and nickel compounds

§12709. Exposure to Trace Elements.

(a) Except where a specific regulatory level is established in Section 12705, exposure to a trace element listed in (b) shall be deemed to pose no significant cancer risk so long as the reasonably anticipated level of exposure to the chemical does not exceed the level set forth in (b).

(b) Element	No Significant Risk Level in micrograms per day
Arsenic (inorganic)	10 (except inhalation)
Beryllium	0.1

§12711. Levels Based on State or Federal Standards.

(a) Except as otherwise provided in section 12705, 12707, 12709, or 12713, levels of exposure deemed to pose no significant risk may be determined as follows:

(1) Where a state or federal agency has developed a regulatory level for a chemical known to the state to cause cancer which is calculated to result in not more than one excess case of cancer in an exposed population of 100,000, such level shall constitute the no significant risk level.

(2) For drinking water, the following levels shall be deemed to pose no significant risk:

(A) Drinking water maximum contaminant levels adopted by the Department of Health Services for chemicals known to the state to cause cancer;

(B) Drinking water action levels for chemicals known to the state to cause cancer for which maximum contaminant levels have not been adopted;

(C) Specific numeric levels of concentration for chemicals known to the state to cause cancer which are permitted to be discharged or released into sources of drinking water by a Regional Water Quality Control Board in a water quality control plan or in waste discharge requirements, when such levels are based on considerations of minimizing carcinogenic risks associated with such discharge or release.

## Article 8. No Observable Effect Levels

§12801. General.

(a) The determination of whether a level of exposure to a chemical known to the state to cause reproductive toxicity has no observable effect for purposes of Health and Safety Code Section 25249.10(c) shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for the listing of a chemical as known to the state to cause reproductive toxicity. Nothing in this article shall preclude a person from using evidence, standards, assessment methodologies, principles, assumptions or levels not described in this article to establish that a level of exposure has no observable effect at one thousand (1,000) times the level in question.

(b) A level of exposure to a listed chemical shall be deemed to have no observable effect, assuming exposure at one thousand times that level, provided that the level is determined:

(1) By means of an assessment that meets the standards described in section 12803 to determine the maximum dose level having no observable effect, and dividing that level by one thousand (1,000) to arrive at the maximum allowable dose level; or

(2) By application of a specific regulatory level for the chemical in question as provided in Section 12805.

(c) For purposes of this article, "NOEL" shall mean that no observable effect level, which is the maximum dose level at which a chemical has no observable reproductive effect.

(d) The chemicals specifically contained in this article do not include all listed reproductive toxicants for which there is a level of exposure which has no observable effect assuming exposure at one thousand times the level in question. The fact that a chemical does not specifically appear in this article does not mean that it has an observable effect at any level.

(e) This article establishes exposure levels solely for purposes of Health and Safety Code Section 25249.10(c). Nothing in this article shall be construed to establish exposure levels for other regulatory purposes.

§12803. Assessment.

(a) A quantitative risk assessment which conforms to this section shall be deemed to determine the level of exposure to a listed chemical which has no observable effect, assuming exposure at one thousand times the level in question. The assessment shall be based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for listing the chemical as known to the state to cause reproductive toxicity. In the absence of principles or assumptions scientifically more appropriate, based upon the available data, the following default principles and assumptions shall apply in any such assessment:

(1) Only studies producing the reproductive effect which provides the basis for the determination that a chemical is known to the state to cause reproductive toxicity shall be utilized for the determination of the NOEL. Where multiple reproductive effects provide the basis for the determination that a chemical is known to the state to cause reproductive toxicity, the reproductive effect for which studies produce the lowest NOEL shall be utilized for the determination of the NOEL. The NOEL shall be the highest dose level which results in no observable reproductive effect, expressed in milligrams of chemical per kilogram of bodyweight per day.

(2) The quality and suitability of available epidemiologic data shall be appraised to determine whether the study is appropriate as the basis of an assessment considering such factors as the selection of the exposed and reference groups, the reliable ascertainment of exposure, and completeness of follow-up. Biases and confounding factors shall be identified and quantified.

(3) Animal bioassay studies for assessment shall meet generally accepted scientific principles, including the thoroughness of experimental protocol, the degree to which dosing resembles the expected manner of human exposure, the temporal exposure pattern, the duration of study, the purity of test material, the number and size of exposed groups, and the route of exposure and the extent of occurrence of effects.

(4) The NOEL shall be based on the most sensitive study deemed to be of sufficient quality.

(5) The results obtained for the most sensitive study deemed to be of sufficient quality shall be applicable to all routes of exposure for which the results are relevant.

(6) When available data are of such quality that anatomic, physiologic, pharmacokinetic and metabolic considerations can be taken into account with confidence, they may be used in the assessment.

(7) When data do not allow the determination of a NOEL, the lowest observable effect level (LOEL) shall be divided by 10 to establish a NOEL for purposes of assessment.

(b) The NOEL shall be converted to a milligram per day dose level by multiplying the assumed human body weight by the NOEL. When the applicable reproductive effect is upon the male, human body weight of 70 kilograms shall be assumed. When the applicable reproductive effect is upon the female or conceptus, human body weight of 58 kilograms shall be assumed.

§12805. Specific Regulatory Levels: Reproductive Toxicants.

(a) Exposure to a chemical at a level which does not exceed the level set forth in subsection (b) for such chemical has no observable effect assuming exposure at one thousand (1,000) times that level.

(b) Chemical Name	Level (Micrograms/day)
Ethylene Oxide	20.0
Lead	0.5
Toluene	7000

(c) Unless a specific level is otherwise provided in this section, an assessment by an agency of the state or federal government that is the substantial equivalent of the assessment described in subdivision (a) of Section 12803, and establishes a maximum allowable daily dose level in the manner provided in paragraph (b)(1) of Section 12801, shall constitute the allowable daily dose level having no observable effect within the meaning of Health and Safety Code Section 25249.10(c).

**Appendix II**  
**Proposition 65 Status Report:**

**No Significant Risk Levels for Carcinogens and  
Maximum Allowable Daily Levels for Chemicals Causing  
Reproductive Toxicity**

**October 2000**

**Reproductive and Cancer Hazard Assessment Section, Office of  
Environmental Health Hazard Assessment, California Environmental  
Protection Agency**

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## Proposition 65 Safe Harbor Levels Development

The Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency is the lead agency for the implementation of the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65 or the Act). In that role, OEHHA has developed Proposition 65 safe harbor levels -- no significant risk levels (NSRLs) for carcinogens and maximum allowable daily levels (MADLs) for chemicals that cause reproductive toxicity. The NSRL is the daily intake level calculated to result in one excess case of cancer in an exposed population of 100,000, assuming lifetime (70-year) exposure at the level in question. The MADL is the level at which the chemical would have no observable adverse reproductive effect assuming exposure at 1,000 times that level. The NSRLs and MADLs are promulgated in Title 22 California Code of Regulations (CCR) Sections 12705 and 12805 to assist interested parties in determining whether warnings are required for exposures to listed chemicals, and whether discharge is prohibited.

This document provides the status of the development and adoption of daily intake levels calculated for all chemicals on the Proposition 65 list. In units of micrograms per day ( $\mu\text{g/day}$ ), Part A reports adopted NSRLs in regulation and Part B reports adopted MADLs for chemicals that cause reproductive toxicity.

Parts C and D of this document give priority levels for development of dose response assessments for chemicals that cause cancer and reproductive toxicity. Interested parties are invited to recommend changes in priority levels. OEHHA retains the right to change priorities in response to the nature and availability of scientific information, and resources available, and requests from the public and the Attorney General's office.

Parts C and D also give draft levels available since January 1994. Because considerable time has passed since draft levels were developed, OEHHA will review the basis for the draft numbers, and update analyses as needed, before proposing any level for formal adoption in regulation.

This status report will be updated on a regular basis.

### A. No Significant Risk Levels (NSRLs) Adopted in Regulation for Carcinogens

The table below lists NSRLs for Proposition 65 carcinogens in regulation (22 CCR §12705 and §12709). These levels are intended to provide "safe harbors" for persons subject to the Act, and do not preclude the use of alternative levels that can be demonstrated by their users as being scientifically valid.

A three-tiered procedure for development of NSRLs is currently in place. NSRLs may be based on a *de novo* dose response assessment conducted by OEHHA (22 CCR §12705(b)), an assessment conducted by another state or federal agency (22 CCR §12705(c)), or an expedited process conducted by OEHHA (22 CCR §12705(d)). The last column of the table below indicates which of these processes was used to develop the NSRL for each chemical. NSRLs represent the daily intake level calculated to result in a cancer risk of one excess case of cancer in 100,000 individuals exposed over a 70-year lifetime.

As chemicals are removed from the Proposition 65 list (e.g., allyl chloride and chlorodibromomethane), the regulatory process to remove the safe harbor level from regulation will be initiated.

Carcinogen	Level (µg/day)	22 CCR Section <sup>a</sup>
A-alpha-C (2-Amino-9H-pyrido[2,3-b]indole)	2	12705(d)
Acetaldehyde	90 (inhalation)	12705(c)
Acetamide	10	12705(d)
2-Acetylaminofluorene	0.2	12705(d)
Acrylamide	0.2	12705(c)
Acrylonitrile	0.7	12705(b)
Actinomycin D	0.00008	12705(d)
AF-2; [2-(2-furyl)-3(5-nitro-2-furyl)acrylamide]	3	12705(d)
Aldrin	0.04	12705(b)
Allyl chloride	30	12705(c)
2-Aminoanthraquinone	20	12705(d)
o-Aminoazotoluene	0.2	12705(d)
4-Aminobiphenyl	0.03	12705(d)
3-Amino-9-ethylcarbazole hydrochloride	9	12705(d)
1-Amino-2-methylanthraquinone	5	12705(d)
2-Amino-5-(5-nitro-2-furyl)-1,3,4-thiadiazole	0.04	12705(d)
Amitrole	0.7	12705(d)
Aniline	100	12705(c)
o-Anisidine	5	12705(d)
o-Anisidine hydrochloride	7	12705(d)
Aramite	20	12705(d)
Arsenic	0.06 (inh) 10 (except inh)	12705(b) 12709
Asbestos	100 fibers <sup>b</sup> /day (inh)	12705(b)
Auramine	0.8	12705(d)
Azaserine	0.06	12705(d)
Azathioprine	0.4	12705(d)
Azobenzene	6	12705(c)
Benzene	7	12705(b)
Benzidine	0.001	12705(b)
Benzo[a]pyrene	0.06	12705(c)
Benzyl chloride	4	12705(c)
Benzyl violet 4B	30	12705(d)
Beryllium	0.1	12709
Beryllium oxide	0.1	12705(c)
Beryllium sulfate	0.0002	12705(c)
Bis(2-chloroethyl)ether	0.3	12705(b)
Bis(chloromethyl)ether	0.02	12705(b)
Bromodichloromethane	5	12705(c)
1,3-Butadiene	0.4	12705(c)
Butylated hydroxyanisole	4000	12705(b)
beta-Butyrolactone	0.7	12705(d)
Cadmium	0.05 (inh)	12705(b)
Captafol	5	12705(d)

a. Section of Title 22, California Code of Regulations (CCR), under which the NSRL is given.

b. Fibers equal to or greater than 5 micrometers in length and 0.3 micrometers in width, with a length/width ratio greater than or equal to 3:1 as measured by phase contrast microscopy.

Captan	300	12705(d)
Carbon tetrachloride	5	12705(b)
Chlorambucil	0.002	12705(d)
Chlordane	0.5	12705(c)
Chlordecone (Kepone)	0.04	12705(d)
Chlorendic acid	8	12705(d)
Chlorinated paraffins (Ave. chain length C12; approx. 60% chlorine by weight)	8	12705(d)
Chlorodibromomethane	7	12705(d)
Chloroform	20 (oral)	12705(c)
	40 (inh)	12705(c)
Chloromethyl methyl ether (technical grade)	0.3	12705(d)
3-Chloro-2-methylpropene	5	12705(d)
4-Chloro-ortho-phenylenediamine	40	12705(d)
Chlorothalonil	200	12705(d)
p-Chloro-ortho-toluidine	3	12705(d)
Chlorozotocin	0.003	12705(d)
Chromium (hexavalent)	0.001 (inh)	12705(b)
C.I. Basic Red 9 monohydrochloride	3	12705(d)
Cinnamyl anthranilate	200	12705(d)
Coke oven emissions	0.3	12705(c)
p-Cresidine	5	12705(d)
Cupferron	3	12705(d)
Cyclophosphamide (anhydrous)	1	12705(d)
Cyclophosphamide (hydrated)	1	12705(d)
D&C Red No. 9	100	12705(d)
Dacarbazine	0.01	12705(d)
Daminozide	40	12705(d)
Dantron (Chrysazin; 1,8-Dihydroxyanthraquinone)	9	12705(d)
DDT, DDE, DDD (in combination)	2	12705(b)
DDVP (Dichlorvos)	2	12705(c)
2,4-Diaminoanisole	30	12705(d)
2,4-Diaminoanisole sulfate	50	12705(d)
4,4'-Diaminodiphenyl ether (4,4'-Oxydianiline)	5	12705(d)
2,4-Diaminotoluene	0.2	12705(d)
Dibenz[a,h]anthracene	0.2	12705(d)
1,2-Dibromo-3-chloropropane	0.1	12705(b)
p-Dichlorobenzene	20	12705(b)
3,3'-Dichlorobenzidine	0.6	12705(b)
1,1-Dichloroethane	100	12705(d)
1,2-Dichloroethane (Ethylene dichloride)	10	12705(b)
Dichloromethane (Methylene chloride)	200 (inh)	12705(b)
	50	12705(c)
Dieldrin	0.04	12705(b)
Di(2-ethylhexyl)phthalate	80	12705(c)
Diethylstilbesterol	0.002	12705(d)
Diglycidyl resorcinol ether (DGRE)	0.4	12705(d)
Dihydrosafrole	20	12705(d)
4-Dimethylaminoazobenzene	0.2	12705(d)
trans-2-[(Dimethylamino)methylimino]-5- [2-(5-nitro-2-furyl)vinyl]-1,3,4-oxadiazole	2	12705(d)
7,12-Dimethylbenz(a)anthracene	0.003	12705(d)
Dimethylcarbamoyl chloride	0.05	12705(d)

1,2-Dimethylhydrazine	0.001	12705(d)
Dimethylvinylchloride	20	12705(d)
2,4-Dinitrotoluene	2	12705(c)
1,4-Dioxane	30	12705(b)
Direct Black 38 (technical grade)	0.09	12705(d)
Direct Blue 6 (technical grade)	0.09	12705(d)
Direct Brown 95 (technical grade)	0.1	12705(d)
Disperse Blue 1	200	12705(d)
Epichlorohydrin	9	12705(b)
Estradiol 17b	0.02	12705(d)
Ethyl-4,4'-dichlorobenzilate (Chlorobenzilate)	7	12705(d)
Ethylene dibromide	0.2 (oral)	12705(b)
	3 (inh)	12705(b)
Ethylene oxide	2	12705(b)
Ethylene thiourea	20	12705(d)
Ethyleneimine	0.01	12705(d)
Folpet	200	12705(c)
Formaldehyde (gas)	40	12705(c)
2-(2-Formylhydrazino)-4-(5-nitro-2-furyl)thiazole	0.3	12705(d)
Furmecyclox	20	12705(c)
Glu-P-1 (2-Amino-6-methyldipyrdo[1,2-a:3',2'-d]imidazole)	0.1	12705(d)
Glu-P-2 (2-Aminodipyrdo[1,2-a:3',2'-d]-imidazole)	0.5	12705(d)
Gyromitrin (Acetaldehyde methylformylhydrazone)	0.07	12705(d)
HC Blue 1	10	12705(d)
Heptachlor	0.2	12705(c)
Heptachlor epoxide	0.08	12705(c)
Hexachlorobenzene	0.4	12705(b)
Hexachlorocyclohexane		
alpha isomer	0.3	12705(c)
beta isomer	0.5	12705(c)
gamma isomer	0.6	12705(c)
technical grade	0.2	12705(b)
Hexachlorodibenzodioxin	0.0002	12705(b)
Hexachloroethane	20	12705(d)
Hydrazine	0.04	12705(c)
Hydrazine sulfate	0.2	12705(c)
Hydrazobenzene (1,2-Diphenylhydrazine)	0.8	12705(d)
IQ (2-Amino-3-methylimidazo[4,5-f]quinoline)	0.5	12705(d)
Lasiocarpine	0.09	12705(d)
Lead acetate	3	12705(d)
Lead subacetate	20	12705(d)
Me-A-alpha-C (2-Amino-3-methyl-9H-pyrido[2,3-b]indole)	0.6	12705(d)
Melphalan	0.005	12705(d)
3-Methylcholanthrene	0.03	12705(d)
4,4'-Methylene bis(2-chloroaniline)	0.5	12705(d)
4,4'-Methylene bis(N,N-dimethyl)benzeneamine	20	12705(c)
4,4'-Methylene bis(2-methylaniline)	0.8	12705(d)

4,4'-Methylenedianiline	0.4	12705(d)
4,4'-Methylenedianiline dihydrochloride	0.6	12705(d)
Methyl methanesulfonate	7	12705(d)
2-Methyl-1-nitroanthraquinone (of uncertain purity)	0.2	12705(d)
N-Methyl-N'-nitro-N-nitrosoguanidine	0.08	12705(d)
Methylthiouracil	2	12705(d)
Michler's ketone	0.8	12705(d)
Mirex	0.04	12705(d)
Mitomycin C	0.00009	12705(d)
Monocrotaline	0.07	12705(d)
2-Naphthylamine	0.4	12705(d)
Nickel refinery dust	0.8	12705(c)
Nickel subsulfide	0.4	12705(c)
Nitrilotriacetic acid	100	12705(d)
Nitrilotriacetic acid, trisodium salt monohydrate	70	12705(d)
5-Nitroacenaphthene	6	12705(d)
5-Nitro-o-anisidine	10	12705(d)
Nitrofen (technical grade)	9	12705(d)
Nitrofurazone	0.5	12705(d)
1-[(5-Nitrofurfurylidene)-amino]-2-imidazolidinone	0.4	12705(d)
N-[4-(5-Nitro-2-furyl)-2-thiazolyl]acetamide	0.5	12705(d)
N-Nitrosodi-n-butylamine	0.06	12705(b)
N-Nitrosodiethanolamine	0.3	12705(c)
N-Nitrosodiethylamine	0.02	12705(b)
N-Nitrosodimethylamine	0.04	12705(b)
p-Nitrosodiphenylamine	30	12705(d)
N-Nitrosodiphenylamine	80	12705(b)
N-Nitrosodi-n-propylamine	0.1	12705(b)
N-Nitroso-N-ethylurea	0.03	12705(b)
N-Nitrosomethylethylamine	0.03	12705(c)
N-Nitroso-N-methylurea	0.006	12705(b)
N-Nitroso-N-methylurethane	0.006	12705(d)
N-Nitrosomorpholine	0.1	12705(d)
N-Nitrosornicotine	0.5	12705(d)
N-Nitrosopiperidine	0.07	12705(d)
N-Nitrosopyrrolidine	0.3	12705(c)
Pentachlorophenol	40	12705(c)
Phenacetin	300	12705(d)
Phenazopyridine	4	12705(d)
Phenazopyridine hydrochloride	5	12705(d)
Phenesterin	0.005	12705(d)
Phenobarbital	2	12705(d)
Phenoxybenzamine	0.2	12705(d)
Phenoxybenzamine hydrochloride	0.3	12705(d)
o-Phenylphenate, sodium	200	12705(d)
Polybrominated biphenyls	0.02	12705(b)
Polychlorinated biphenyls	0.09	12705(c)
Ponceau MX	200	12705(d)
Ponceau 3R	40	12705(d)
Potassium bromate	1	12705(d)
Procarbazine	0.05	12705(d)
Procarbazine hydrochloride	0.06	12705(d)

1,3-Propane sultone	0.3	12705(d)
beta-Propiolactone	0.05	12705(d)
Propylthiouracil	0.7	12705(d)
Reserpine	0.06	12705(d)
Safrole	3	12705(d)
Sterigmatocystin	0.02	12705(d)
Streptozotocin	0.006	12705(d)
Styrene oxide	4	12705(d)
Sulfallate	4	12705(d)
Tetrachlorodibenzo-p-dioxin	0.000005	12705(b)
1,1,2,2-Tetrachloroethane	3	12705(d)
Tetrachloroethylene	14	12705(c)
Thioacetamide	0.1	12705(d)
4,4'-Thiodianiline	0.05	12705(d)
Thiourea	10	12705(d)
Toluene diisocyanate	20	12705(d)
ortho-Toluidine	4	12705(d)
ortho-Toluidine hydrochloride	5	12705(d)
Toxaphene	0.6	12705(b)
Trichloroethylene	50 (oral)	12705(b)
	80 (inh)	12705(b)
2,4,6-Trichlorophenol	10	12705(b)
Tris(1-aziridiny)phosphine sulfide (Thiotepa)	0.06	12705(d)
Tris(2,3-dibromopropyl)phosphate	0.3	12705(d)
Trp-P-1 (Tryptophan-P-1)	0.03	12705(d)
Trp-P-2 (Tryptophan-P-2)	0.2	12705(d)
Urethane (Ethyl carbamate)	0.7	12705(b)
Vinyl chloride	3	12705(b)
Vinyl trichloride (1,1,2-Trichloroethane)	10	12705(d)

## B. Maximum Allowable Daily Levels (MADLs) Adopted in Regulation for Chemicals Causing Reproductive Toxicity

The following table is a compilation of MADLs in regulation (22 CCR §12805) for Proposition 65 chemicals that cause reproductive toxicity. These levels represent the no observable effect level (NOEL) for the chemical, divided by 1,000. NOELs are set in accordance with procedures specified in 22 CCR §12803.

Chemical Listed as Causing Reproductive Toxicity	Level (µg/day)
Ethylene oxide	20
Lead	0.5
Toluene	7000 <sup>c</sup>

## C. Priority List for the Development of NSRLs for Proposition 65 Carcinogens

OEHHA has developed the following priority list, which classifies into four priorities carcinogens for which dose-response assessments have not been completed. Priority levels reflect the availability and quality of scientific data for dose-response assessments, potential for exposure, resources available to perform the assessment, commitments made in settlement of the case of AFL-CIO v. Deukmejian (Sacramento Superior Court No. 3481295) and input from the public and Attorney General's office. OEHHHA anticipates proposing NSRLs for the majority of chemicals in the first priority group within the next two years, and for second priority chemicals within the next two to four years. It is unlikely that NSRLs for chemicals in third and fourth priority chemicals would be released within the next three years.

Any interested party may submit recommendations to OEHHHA for revising the priority assignment for any of the chemicals listed. Recommendations should be accompanied by appropriate documentation supporting the alternative priority assignment suggested. OEHHHA expects changes in priorities resulting from the availability of scientific information and resources, and requests from the public and Attorney General's office.

A three-tiered procedure for development of NSRLs is currently in place. NSRLs may be based on a *de novo* dose response assessment conducted by OEHHHA (22 CCR §12705(b)), an assessment conducted by another state or federal agency (22 CCR §12705(c)), or an expedited process conducted by OEHHHA (22 CCR §12705(d)). The table below indicates draft NSRLs released in January 1994 or before, along with the procedures used to develop the value. Because considerable time has passed since these draft levels were developed, OEHHHA will review the basis for the draft numbers, and update analyses as needed, before proposing any level for formal adoption in regulation.

### 1. First Priority

Acetochlor	(draft NSRL: 70 µg/day [12705(b)])
Acifluorfen	(draft NSRL: 20 µg/day [12705(c)])
Alachlor	(draft NSRL: 9 µg/day [12705(c)])
1-Amino-2,4-dibromoanthraquinone	
Aniline hydrochloride	
Antimony oxide	
Azacitidine	

- c. Level represents absorbed dose (rounded from 6,525 µg/day). Since absorption of ingested toluene is at 100%, absorbed oral dose is equivalent to administered dose. On the other hand, the rate of absorption of toluene via inhalation is assumed to be at 50 percent, producing an administered dose which is twice the oral exposure value (i.e., 13,050 µg/day rounded off to 13,000 µg/day).

Benz[a]anthracene	(draft NSRL: 0.04 µg/day [12705(b)])
Benzo[b]fluoranthene	(draft NSRL: 0.04 µg/day [12705(b)])
Benzo[j]fluoranthene	(draft NSRL: 0.09 µg/day [12705(b)])
Benzo[k]fluoranthene	
Benzofuran	(draft NSRL: 1 µg/day [12705(b)])
Benzotrichloride	(draft oral NSRL: 0.05 µg/day [12705(c)]) (draft NSRL: 0.0002 µg/day [12705(b)])
2,2-Bis(bromomethyl)-1,3-propanediol	
Bromoform	(draft NSRL: 90 µg/day [12705(c)])
Carbazole	
<i>p</i> -Chloroaniline	
<i>p</i> -Chloroaniline hydrochloride	
Chlordimeform	(draft NSRL: 0.5 µg/day [12705(c)])
Chloroethane (Ethyl chloride)	(draft NSRL: 200 µg/day [12705(b)])
<i>p</i> -Chloro- <i>o</i> -toluidine, strong acid salts of	
Chrysene	(draft NSRL: 0.2 µg/day [12705(b)])
C. I. Acid Red 114	
C.I. Direct Blue 15	
C.I. Direct Blue 218	
C.I. Solvent Yellow 14	
Dibenz[a,h]acridine	
Dibenz[a,j]acridine	
Dibenzo[a,e]pyrene	
Dibenzo[a,h]pyrene	(draft NSRL: 0.002 µg/day [12705(b)])
Dibenzo[a,i]pyrene	(draft NSRL: 0.002 µg/day [12705(b)])
Dibenzo[a,l]pyrene	
7H-Dibenzo[c,g]carbazole	(draft NSRL: 0.0009 µg/day [12705(b)])
3,3'-Dichlorobenzidine dihydrochloride	
1,2-Dichloropropane	
1,3-Dichloropropene	(draft oral NSRL: 4 µg/day [12705(b)]) (draft inhalation NSRL: 20 µg/day [12705(c)])
Diepoxybutane	
Diethyl sulfate	(draft NSRL: 0.7 µg/day [12705(b)])
3,3'-Dimethoxybenzidine dihydrochloride	(draft NSRL: 0.2 µg/day [12705(b)])
3,3'-Dimethoxybenzidine (o-Dianisidine)	(draft NSRL: 0.1 µg/day [12705(b)])
Dimethyl sulfate	(draft NSRL: 0.05 µg/day [12705(b)])
3,3'-Dimethylbenzidine dihydrochloride	(draft NSRL: 0.01 µg/day [12705(b)])
3,3'-Dimethylbenzidine (o-Toluidine)	(draft NSRL: 0.009 µg/day [12705(b)])
1,1-Dimethylhydrazine (UDMH)	(draft NSRL: 0.3 µg/day [12705(b)])
1,6-Dinitropyrene	(draft NSRL: 0.02 µg/day [12705(b)])
1,8-Dinitropyrene	(draft NSRL: 0.01 µg/day [12705(b)])
2,6-Dinitrotoluene	
Ethinylestradiol	
Ethylene thiourea	(draft NSRL: 30 µg/day [12705(b)])
Furan	
Glycidol	(draft NSRL: 0.4 µg/day [12705(b)])
Griseofulvin	(draft NSRL: 50 µg/day [12705(b)])
Hexamethylphosphoramide	(draft NSRL: 0.01 µg/day [12705(b)])
Indeno[1,2,3-cd]pyrene	
Isobutyl nitrite	
Isoprene	
Lactofen	(draft NSRL: 4 µg/day [12705(c)])
Lead	



Lead phosphate	
MeIQ(2-Amino-3,4-dimethylimidazo[4,5-f]quinoline)	
MeIQx(2-Amino-3,8-dimethylimidazo[4,5-f]quinoxaline)	
Methyl carbamate	
Methyl iodide	
2-Methylaziridine (Propyleneimine)	(draft NSRL: 0.03 µg/day [12705(b)])
5-Methylchrysene	(draft NSRL: 0.005 µg/day [12705(b)])
Methylhydrazine	(draft NSRL: 0.6 µg/day [12705(b)])
Methylhydrazine sulfate	(draft NSRL: 0.2 µg/day [12705(b)])
Metronidazole	(draft NSRL: 4 µg/day [12705(b)])
5-(Morpholinomethyl)-3-[(5-nitrofurfurylidene)- amino]-2-oxalolidinone	(draft NSRL: 0.2 µg/day [12705(b)])
Nafenopin	
Nalidixic acid	
Nickel carbonyl	
o-Nitroanisole	
Nitrobenzene	
4-Nitrobiphenyl	
6-Nitrochrysene	(draft NSRL: 0.002 µg/day [12705(b)])
2-Nitrofluorene	(draft NSRL: 0.09 µg/day [12705(b)])
2-Nitropropane	(draft NSRL: 30 µg/day [12705(b)])
1-Nitropyrene	(draft NSRL: 0.6 µg/day [12705(b)])
4-Nitropyrene	(draft NSRL: 0.03 µg/day [12705(b)])
N-Methylolacrylamide	(draft NSRL: 2 µg/day [12705(b)])
4-(N-Nitrosomethylamino)-1-(3-pyridyl)1-butanone	
N-Nitrosomethylvinylamine	(draft NSRL: 0.004 µg/day [12705(b)])
N-Nitrososarcosine	(draft NSRL: 5 µg/day [12705(b)])
Ochratoxin A	(draft NSRL: 0.03 µg/day [12705(b)])
Oxazepam	
o-Phenylenediamine and its salts	
Phenyl glycidyl ether	(draft NSRL: 5 µg/day [12705(b)])
Phenylhydrazine	(draft NSRL: 0.6 µg/day [12705(b)])
Phenylhydrazine hydrochloride	(draft NSRL: 0.8 µg/day [12705(b)])
o-Phenylphenol	
PhiP	
Poligeenan	(draft NSRL: 200 µg/day [12705(b)])
Pronamide	
Saccharin	(draft NSRL: 2800 to 840000 µg/day <sup>d</sup> [12705(b)])
Saccharin, sodium	(draft NSRL: 2800 to 840000 µg/day <sup>d</sup> [12705(b)])
Selenium sulfide	
Tetranitromethane	(draft NSRL: 0.05 µg/day [12705(b)])
1,2,3-Trichloropropane	
Trimethyl phosphate	
Tris(2-chloroethyl)phosphate	
Vinyl bromide	(draft oral NSRL: 1 µg/day [12705(b)]) (draft inhalation NSRL: 4 µg/day [12705(b)])
4-Vinylcyclohexene	
2,6-Xylidine	(draft NSRL: 100 µg/day [12705(b)])

d. OEHHA evaluated several possible approaches for deriving NSRLs for saccharin and sodium saccharin. The range corresponds to the options considered. If the evidence supports a finding that saccharin is carcinogenic by a species-specific mechanism of action, further alternative approaches to deriving NSRLs will be considered.

It is anticipated that proposed changes to NSRLs will be released during the next year for the following chemicals:

Benzene  
Chromium (VI)  
Di(2-ethylhexyl)phthalate  
Lead acetate  
Lead subacetate  
Pentachlorophenol  
Tetrachloroethylene

2. Second Priority

Aflatoxins (draft NSRL: 0.02 µg/day [12705(b)])  
*p*-Aminoazobenzene  
Bis(2-chloro-1-methylethyl)ether, technical grade  
Cacodylic acid  
Ceramic fibers (airborne particles of respirable size)  
1-Chloro-4-nitrobenzene  
Chloroprene  
5-Chloro-*o*-toluidine and its strong acid salts  
Cobalt metal powder  
Cobalt [II] oxide  
Cobalt sulfate heptahydrate  
Diaminotoluene (mixed)  
2,3-Dibromo-1-propanol  
Dichloroacetic acid  
1,4-Dichloro-2-butene  
Diesel engine exhaust  
Di-*n*-propyl isocinchomeronate (MGK Repellent 326)  
Estragole  
Fenoxycarb  
Iprodione  
Isosafrole  
Metham sodium  
1-Naphthylamine  
Nickel and nickel compounds  
Nitromethane  
*o*-Nitrotoluene  
Oxadiazon  
Oxythioquinox  
Primidone  
Quinoline and its strong acid salts  
Salicylazosulfapyridine  
Silica, crystalline (airborne particles of respirable size)  
Testosterone and its esters  
*p*-a,a,a-Tetrachlorotoluene  
Tetrafluoroethylene  
2,4,5-Trimethylaniline and its strong acid salts  
Triphenyltin hydroxide  
Trypan blue (commercial grade)  
4-Vinyl-1-cyclohexene diepoxide

3. Third Priority

Adriamycin (Doxorubicin hydrochloride)  
Benzidine-based dyes  
N,N-Bis(2-chloroethyl)-2-naphthylamine  
Bischloroethyl nitrosourea (BCNU) (Carmustine)  
1,4-Butanediol dimethanesulfonate (Busulfan)  
Chloramphenicol  
1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU)  
1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea  
Chlorotrianisene  
Ciclosporin (Cyclosporin A; Cyclosporine)  
Cidofovir  
Cisplatin  
Clofibrate  
Daunomycin  
N,N'-Diacetylbenzidine  
3,3'-Dichloro-4,4'-diaminodiphenyl ether  
Dienestrol  
1,2-Diethylhydrazine  
Diisopropyl sulfate  
2,4-/2,6-Dinitrotoluene mixture  
Diphenylhydantoin (Phenytoin)  
Diphenylhydantoin (Phenytoin), sodium salt  
Estrone  
Estropipate  
Ethyl acrylate  
Furazolidone  
Fusarin C  
Ganciclovir sodium  
Gasoline engine exhaust (condensates/extracts)  
Glasswool fibers (airborne particles of respirable size)  
Glycidaldehyde  
Mancozeb  
Maneb  
Medroxyprogesterone acetate  
Merphalan  
Mestranol  
Methyl iodide  
Metiram  
Mustard Gas  
Nickel carbonyl  
Niridazole  
Nitrogen mustard (Mechlorethamine)  
Nitrogen mustard hydrochloride (Mechlorethamine HCl)  
Nitrobiphenyl  
Norethisterone (Norethindrone)  
Oxymetholone  
Panfuran S  
Polychlorinated dibenzofurans  
Polychlorinated dibenzo-p-dioxins  
Propylene oxide (draft oral NSRL: 3 µg/day [12705(c)])  
(draft inhalation NSRL: 60 µg/day [12705(c)])

Procymidone  
Propargite  
Progesterone  
Radionuclides  
Spironolactone  
Stanozolol  
Tamoxifen and its salts  
Terrazole  
Thiodicarb  
Thorium dioxide  
Treosulfan  
Trichlormethine (Trimustine hydrochloride)  
Uracil mustard  
Vinclozolin  
Vinyl fluoride

4. Fourth Priority

Alcoholic beverages  
2-Aminofluorene  
4-Amino-2-nitrophenol  
Analgesic mixtures containing phenacetin  
Betel quid with tobacco  
Bitumens, extracts of steam-refined  
Bracken fern  
Caffeic Acid  
Carbon-black extracts  
Certain combined chemotherapy for lymphomas  
Citrus Red No. 2  
Conjugated estrogens  
Creosotes  
Cycasin  
Cytembena  
D&C Orange No. 17  
D&C Red No. 8  
D&C Red No. 19  
3,7-Dinitrofluoranthene  
3,9-Dinitrofluoranthene  
Erionite  
Ethyl methanesulfonate  
Iron dextran complex  
8-Methoxypsoralen with ultraviolet A therapy  
5-Methoxypsoralen with ultraviolet A therapy  
Methylazoxymethanol  
Methylazoxymethanol acetate  
Methylmercury compounds  
Nitrogen mustard N-oxide  
Nitrogen mustard N-oxide hydrochloride  
3-(N-Nitrosomethylamino)propionitrile  
Oil Orange SS  
Oral contraceptives, combined  
Oral contraceptives, sequential  
Palygorskite fibers  
Phenolphthalein

- Residual (heavy) fuel oils
- Shale-oils
- Soots, tars, and mineral oils
- Talc containing asbestiform fibers
- Tobacco, oral use of smokeless products
- Tobacco smoke
- Tris(aziridiny)l-para-benzoquinone (Triaziquone)
- Unleaded gasoline (wholly vaporized)

#### **D. Priority List for the Development of Maximum Allowable Daily Levels (MADLs) for Chemicals Causing Reproductive Toxicity**

OEHHA has developed the following priority list, which divides chemicals causing reproductive toxicity for which dose-response assessments have not been completed into three priorities. Priority levels reflect the availability and quality of scientific data for dose-response assessments, potential for exposure, resources available to perform the assessment, and input from the public and the Attorney General's office. OEHHA anticipates proposing MADLs for the majority of chemicals in the first priority group within the next two years, and for several chemicals in the second priority within the next two to four years. It is unlikely that MADLs for chemicals in the third priority group would be released within the next three years.

Any interested party may submit recommendations to OEHHA on revising the priority assignment for any of the chemicals listed. Recommendations should be accompanied by appropriate documentation supporting the alternative priority assignment suggested. OEHHA expects changes in priorities resulting from the availability of scientific information and resources and requests from the public and Attorney General's office.

Also given below are draft levels available since January 1994. Because considerable time has passed since these levels were developed, OEHHA will review the basis for the draft numbers, and update analyses as needed, before proposing any level for formal adoption in regulation.

##### **1. First Priority**

Arsenic (inorganic oxides)	
Benzene	
Cadmium	
Carbon disulfide	(draft oral MADL: 600 µg/day [12805])
	(draft inhalation MADL: 1000 µg/day [12805])
1,2-Dibromo-3-chloropropane (DBCP)	(draft MADL: 5 µg/day [12805])
<i>m</i> -Dinitrobenzene	(draft MADL: 80 µg/day [12805])
Methyl bromide as a structural fumigant	(draft MADL: 1000 µg/day [12805])
Quizalofop-ethyl	

##### **2. Second Priority**

- Amitraz
- Bromacil lithium salt
- Bromoxynil
- Bromoxynil octanoate
- Chinomethionat (Oxythioquinox)
- Chlorsulfuron
- Cocaine

Cycloate  
2,4-D butyric acid  
Diclofop methyl  
Dichlorophene  
Disodium cyanodithiomidocarbonate  
Ethyl dipropylthiocarbamate  
Ethylene glycol monoethyl ether  
Ethylene glycol monomethyl ether  
Ethylene glycol monoethyl ether acetate  
Ethylene glycol monomethyl ether acetate  
Ethylene thiourea  
Fenoxaprop ethyl  
Fluazifop butyl  
Fluvalinate  
Hydramethylnon  
Linuron  
Metham Sodium  
Methazole  
Metiram  
Myclobutanil  
Nabam  
Nicotine  
Nitrpyrin  
Oxydemeton methyl  
Oxadiazon  
Potassium dimethyldithiocarbamate  
Propargite  
Resmethrin  
Sodium dimethyldithiocarbamate  
Sodium fluoroacetate  
Terbacil  
Thiophanate-methyl  
Triadimefon  
Tributyltin methacrylate  
Triforine  
Vinclozolin

3. Third Priority

Acetazolamide  
Acetohydroxamic acid  
Actinomycin D  
All-trans retinoic acid  
Alprazolam  
Altretamine  
Amikacin sulfate  
Aminoglutethimide  
Aminoglycosides  
Aminopterin  
Amiodarone hydrochloride  
Amoxapine  
Anabolic steroids  
Angiotensin converting enzyme (ACE) inhibitors  
Anisindione  
Aspirin

Atenolol  
 Auranofin  
 Azathioprine  
 Barbiturates  
 Beclomethasone dipropionate  
 Benomyl  
 Benzphetamine hydrochloride  
 Benzodiazepines  
 Bischloroethyl nitrosourea (BCNU) (Carmustine)  
 Butabarbital sodium  
 1,4-Butanediol dimethanesulfonate (Busulfan)  
 Carbamazepine  
 Carbon monoxide  
 Carboplatin  
 Chenodiol  
  
 Chlorambucil  
 Chlorcyclizine hydrochloride  
 Chlordecone (Kepone)  
 Chlordiazepoxide  
 Chlordiazepoxide hydrochloride  
 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU) (Lomustine)  
 Cidofovir  
 Cladribine  
 Clarithromycin  
 Clobetasol propionate  
 Clomiphene citrate  
 Clorazepate dipotassium  
 Codeine phosphate  
 Colchicine  
 Conjugated estrogens  
 Cyanazine  
 Cyclohexanol  
 Cycloheximide  
 Cyclophosphamide (anhydrous)  
 Cyclophosphamide (hydrated)  
 Cyhexatin  
 Cytarabine  
 2,4-DP  
 Dacarbazine  
 Danazol  
 Daunorubicin hydrochloride  
*o,p'* -DDT  
*p,p'* -DDT  
 Demeclocycline hydrochloride (internal use)  
 Diazepam  
 1,2-Dibromo-3-chloropropane (DBCP)  
 Dichlorophene  
 Dicumarol  
 Diethylstilbestrol (DES)  
 Diflunisal  
 Dihydroergotamine mesylate  
*m*-Dinitrobenzene  
*o*-Dinitrobenzene

*p*-Dinitrobenzene  
2,4-Dinitrotoluene  
2,6-Dinitrotoluene  
Dinitrotoluene (technical grade)  
Dinocap  
Dinoseb  
Diphenylhydantoin (Phenytoin)  
Doxorubicin hydrochloride  
Doxycycline (internal use)  
Doxycycline calcium (internal use)  
Doxycycline hyclate (internal use)  
Doxycycline monohydrate (internal use)  
Endrin  
Epichlorohydrin  
Ergotamine tartrate  
Estropipate  
Ethionamide  
Ethyl alcohol in alcoholic beverages  
Ethylene dibromide  
Etodolac  
Etoposide  
Etretinate  
Flunisolide  
Fluorouracil  
Fluoxymesterone  
Flurazepam hydrochloride  
Flurbiprofen  
Flutamide  
Fluticasone propionate  
Ganciclovir sodium  
Gemfibrozil  
Goserelin acetate  
Halazepam  
Halobetasol propionate  
Haloperidol  
Halothane  
Heptachlor  
Hexachlorobenzene  
Hexamethylphosphoramide  
Histrelin acetate  
Hydroxyurea  
Idarubicin hydrochloride  
Ifosfamide  
Iodine-131  
Isotretinoin  
Leuprolide acetate  
Levodopa  
Levonorgestrel implants  
Lithium carbonate  
Lithium citrate  
Lorazepam  
Lovastatin  
Mebendazole  
Medroxyprogesterone acetate



Megestrol acetate  
Melphalan  
Menotropins  
Meprobamate  
Mercaptopurine  
Mercury and mercury compounds  
Methacycline hydrochloride  
Methimazole  
Methotrexate  
Methotrexate sodium  
Methyl chloride  
Methyl mercury  
Methyltestosterone  
Midazolam hydrochloride  
Minocycline hydrochloride (internal use)  
Misoprostol  
Mitoxantrone hydrochloride  
Nafarelin acetate  
Neomycin sulfate (internal use)  
Netilmicin sulfate  
Nickel carbonyl  
Nifedipine  
Nitrofurantoin  
Nitrogen mustard (Mechlorethamine)  
Nitrogen mustard hydrochloride (Mechlorethamine hydrochloride)  
Norethisterone (Norethindrone)  
Norethisterone acetate (Norethindrone acetate)  
Norethisterone (Norethindrone)/Ethinyl estradiol  
Norethisterone (Norethindrone)/Mestranol  
Norgestrel  
Oxazepam  
Oxymetholone  
Oxytetracycline (internal use)  
Oxytetracycline hydrochloride (internal use)  
Paclitaxel  
Paramethadione  
Penicillamine  
Pentobarbital sodium  
Pentostatin  
Phenacetamide  
Phenprocoumon  
Pimozide  
Pipobroman  
Pllicamycin  
Polybrominated biphenyls  
Polychlorinated biphenyls  
Pravastatin sodium  
Prednisolone sodium phosphate  
Procarbazine hydrochloride  
Propylthiouracil  
Primethamine  
Quazepam  
Retinol/retinyl esters, when in daily dosages in excess of 10,000 IU, or 3,000 retinol equivalents.

Ribavirin  
Secobarbital sodium  
Sermorelin acetate  
Sulfasalazine  
Streptomycin sulfate  
Streptozocin (streptozotocin)  
Sulindac  
Tamoxifen citrate  
Temazepam  
Teniposide  
Testosterone cypionate  
Testosterone enanthate  
2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)  
Tetracycline (internal use)  
Tetracyclines (internal use)  
Tetracycline hydrochloride (internal use)  
Thalidomide  
Thioguanine  
Tobacco smoke (primary)  
Tobramycin sulfate  
Triazolam  
Trilostane  
Trimethadione  
Trimetrexate glucuronate  
Uracil mustard  
Urethane  
Urofollitropin  
Valproate (Valproic acid)  
Vinblastine sulfate  
Vincristine sulfate  
Warfarin